Pheochromocytoma

A Report of 12 Cases

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• In a series of 12 cases of pheochromocytoma, 11 patients were clinically cured by operation and one died of malignant tumor.

It has been reported that of patients presenting with hypertension, 0.5 to possibly 2 per cent will be found to have pheochromocytoma. This small group of patients will have a good chance of cure of hypertension by surgical removal of the tumor.

Hypertension and manifestations of hypermetabolism are classically seen in pheochromocytoma, but these symptoms vary, and hypertension may be entirely absent.

Hypertension which is no longer dependent on pressor amines may result after prolonged circulation of pressor substances in the bloodstream. The quantity and proportion of the pressor amines in the circulation are largely responsible for the variable clinical picture.

The Regitine® test is an excellent screening test but is not absolutely specific for pheochromocytoma.

The histamine test should not be employed in patients whose blood pressure exceeds 160/110 mm. of mercury, lest it set off cerebrovascular accident.

A modification of the Garlock transdiaphragmatic incision that was used in the present series of cases affords unparalleled exposure and facility in the removal of pheochromocytoma.

THE OCCASIONAL REPORT concerning the clinical features of a particular case of a rare tumor of the endocrine system is likely to lack general interest if it has been established that tumors of the particular kind in question follow a uniform clinical pattern. Certainly pheochromocytoma masquerading as essential or "labile" hypertension, as diabetes mellitus, as thyrotoxicosis or occasionally as a psychoneurosis does not fall into this category. The series of 12 cases here presented is reported in the hope that a more precise clinical picture will eventually be formed.

Pheochromocytoma derives its name (*phaios*, dusky; *chroma*, color) from the dark brown color which most chromaffin tumors assume when treated with potassium dichromate. As a clinical entity, pheochromocytoma is comparatively new, the first case having been reported in 1886 by Fränkel, who observed bilateral adrenal medullary tumors at autopsy in a girl of 18 who died in coma. The first correct preoperative diagnosis and successful removal of a pheochromocytoma is credited to Pincoffs[7] in 1929. In the same year, Rabin determined the amount of epinephrine in a pheochromocytoma and, finding it to be in excess of that in the normal adrenal medulla, ascribed the clinical symptoms to this change.[13]

Pheochromocytoma is relatively rare—a total of approximately 325 cases reported to date. In patients in whom the presenting symptom was hypertension, the incidence was estimated by Smithwick to be 0.5 per cent.[9] Other investigators have thought the incidence in such cases may be 2 per cent or even higher. This constitutes a small, but potentially curable group of hypertensives and is in marked contrast to the balance of patients (except those with unilateral renal artery disease) for whom there remains only palliation. Three instances of pheochromocytoma have been reported in two members of a family, and Roth[8] reported bilateral tumors in three siblings. We include in this series two siblings who had this tumor and whose father had bilateral pheochromocytoma.

SYMPTOMS

In patients with pheochromocytoma the classical presenting feature is paroxysmal or sustained hypertension. Sweating, palpitations, anxiety, severe headache, flushing, nausea and vomiting are frequent symptoms. Other associated phenomena include paresthesias, thoracic or abdominal pain, cold, clammy or blanched extremities, as well as gradual impairment of vision, pronounced congestive failure or cerebrovascular accident which eventually develops unless the tumor is removed. The clinical complex of symptoms is extremely variable; many of the symptoms that are usually present, including hypertension, may be entirely lacking in some cases. A young tumor will generally give rise to less frequent periods of acute symptoms and more clinically dormant phases than an older tumor. After long periods and repeated attacks, the patient may acquire persistent rather than paroxysmal hypertension because of irreversible renal changes.[3] Not only do the duration and frequency of paroxysms influence the symptom complex, but also the probably constantly varying amounts and proportion of the vasospastic hormones play an important role.

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Presented before the Section on Urology at the 88th Annual Session of the California Medical Association, San Francisco, February 22 to 25, 1959.

The frequency of attacks varies from ten or more per day to an isolated episode every few months. Most of the patients in the present series had paroxysms three or four times a week. Paroxysms usually lasted 5 to 10 minutes, occasionally longer, sometimes for only a few seconds. A variety of stimuli causing discharge of pressor amines from the tumor have been observed, among them changes in posture, pressure over the tumor, emotion, overindulgence in eating, shock, sneezing, singing and even voiding.

PATHOPHYSIOLOGY

Epinephrine alone was originally thought to be responsible for the symptoms of pheochromocytoma, this pressor substance being liberated from the adrenal tumor into the circulation. It was soon evident, however, that certain features of a typical attack were not explainable on the basis of the epinephrine effect alone. In 1949 Holton[4] discovered norepinephrine in normal adrenal medullary tissue, as well as in pheochromocytoma; and in the latter, concentration of norepinephrine could exceed that of epinephrine tenfold. Since then, the discovery and differentiation of pressor amines in the circulation have helped to explain the source and mechanism of an individual attack.

Epinephrine alone administered intravenously produces most of the manifestations of a typical paroxysm—abrupt rise in systolic blood pressure, anxiety, mydriasis, blanching of hands and feet, tachycardia, dyspnea and sweating, probably through sympathetic excitation. Norepinephrine in therapeutic doses has been shown to cause an increase in diastolic and systolic blood pressure and bradycardia but with few other subjective symptoms. The attempt at correlation of symptomatology with pressor analysis of the pheochromocytoma was more difficult until Goldenberg[2] and co-workers in 1950 demonstrated the difference in response to small and large doses of the two amines given intravenously to dogs. This study suggested that the tumor's pressor amine secretion could fluctuate in quantity and probably also in quality irrespective of the analysis of pressor content of the tumor, and consequently produce varying symptoms.

Patients with an intermittently discharging pheochromocytoma usually have paroxysmal hypertension, while others with a constant secretion of pressor amines have sustained hypertension. Goldenberg in 1950 found that intermittent or continuous discharge of pressor amines could be associated with persistent hypertension, implying that after prolonged circulation of pressor substances in the blood the ensuing hypertension may no longer depend on the circulating amines.

Symptoms of sustained hypermetabolism but paroxysmal hypertension may be explained on the assumption that a basal epinephrine secretion adequately meets the needs of hypermetabolism but is insufficient to produce the hypertension until epinephrine secretion increases suddenly.[6]

DIAGNOSIS

Pharmacological tests help greatly in the diagnosis of pheochromocytoma. Following the establishment of a patient's base-line blood pressure a cold pressor test is performed, followed by a histamine test. If the systolic and diastolic pressures rise roughly 60 mm. and 30 mm. of mercury, respectively, the result is "positive" provided the readings are in excess of that of the cold pressor test. This comparison will rule out the "hyper-reactor," as shown by Roth and Kvale.[5,8] We restrict the histamine test to patients whose blood pressure does not exceed 160/110 mm. of mercury and thereby reduce the incidence of catastrophes such as cerebrovascular accidents which can result from extreme pressor responses.

Regitine® has been used in most of the cases in this report. We have found it to be an easily administered and safe drug and well suited to a routine screening test. If pheochromocytoma is suspected and the blood pressure exceeds 170/110, Regitine® is the drug of choice for a screening test. The result of the test is "positive" if there is a decrease of more than 35 mm. of mercury in systolic and 25 mm. diastolic readings, both occurring within two minutes after intravenous injection.

The quantitative assay of pressor amines in the blood is the most direct and precise aid at present in diagnosis. The specimen of blood must be taken during or immediately following an acute episode if the results are to be significant. The normal values vary with the different laboratories but generally range from 3.5 to 5 micrograms of norepinephrine and about 0.5 micrograms of epinephrine per liter of blood as upper limits of normal.

During a normotensive phase, a rise in blood pressure may be brought about by the intravenous administration of 0.025 mg. or less of histamine base. If a blood specimen is drawn at the height of the blood pressure rise, levels of catechol amines of more than 20 micrograms per 100 cc. indicates the presence of a pheochromocytoma.

Urinary catechol amines are also of diagnostic significance. They will be found only in specimens taken during a period of active secretion by the pheochromocytoma. In the past these have been reported as total catechol amines assayed by a fluorometric technique. More recently, separate determination of the urinary epinephrine and norepinephrine has become available. Normal excretion should not exceed 50 and 200 micrograms per 100 cc., respectively, for these substances.[2,11,12]

An invaluable aid in the diagnosis of pheochromocytoma is intravenous pyelography. It should be carried out to supply one of the pieces of evidence which should be assembled before diagnosis is made. If the tumor is large enough, it will usually be seen as an ovoid soft tissue mass in the region of the adrenal gland and occasionally overlying a kidney. However, one must be careful not to misinterpret fluid in the stomach as a left suprarenal mass. The tumor will frequently displace the longitudinal calyceal axis of the kidney laterally and inferiorly. We believe that, excepting an obvious adrenal tumor mass seen on pyelography, the described change in axis of the calyces of a kidney, even to a slight degree, is the most suspicious sign of adjacent tumor mass. Calyceal distortion is rarely seen in pheochromocytoma and, barring primary renal lesions, would indicate invasion of renal parenchyma by malignant tumor.

If better delineation of perirenal structures is desired, we have used retroperitoneal oxygen insufflation and tomography with excellent result.[10] If such procedures or the pyelogram localize a suprarenal tumor, they become valuable aids to the surgeon in selection of an operative approach.

In the present series aortography has been employed on one occasion only (Case 7). In that case the procedure localized a very small tumor not seen in pyelographic or in oxygen studies. As a rule aortography is considered to be not without significant hazard in pheochromocytoma, for the added trauma may precipitate a fatal hypertensive attack.

SURGICAL ASPECTS

The recording of the blood pressure of the patient with pheochromocytoma at 1 or 2-minute intervals before and during all phases of anesthesia and operation is imperative and frequently lifesaving. In addition to the anesthetist, one member of a medical team of two persons records the blood pressure and the other controls the intravenous administration of fluids. We have used a blood pressure cuff in the past, but in our most recent case we resorted to a continuous arterial pressure-recording device, which necessitated brachial arteriotomy and catheterization. The removal of the pheochromocytoma in that case was uneventful. However, in the evening of the operation the patient complained of severe ischemic pain in the forearm, and the radial and ulnar pulses were absent. When an arteriogram revealed a complete block in the brachial artery just proximal to the bifurcation, the artery was again opened and thrombectomy performed. Following this the edema, numbness and duskiness of the hand and forearm gradually resolved. While arteriotomy is usually not considered a hazardous procedure, we feel that the intermittent blood pressure recording with a cuff is more than adequate and entails no risk whatsoever.

During the period between induction of anesthesia and the postoperative phase, the blood pressure is controlled by intravenous administration of Regitine® or Levophed® (L-norepinephrine) or 5 per cent dextrose and water, as needed. Characteristically, the blood pressure fluctuates throughout operation, rising perhaps with induction of anesthesia or the skin incision. A maximal rise usually occurs as the tumor is palpated and sporadic decreases then occur as the veins of the tumor are ligated. Pronounced hypotension is usually noted on removal of the tumor.

We favor the Garlock transdiaphragmatic approach for a pheochromocytoma that is demonstrated radiographically to be unilateral. Our modification of this incision is to make it between the ninth and tenth ribs with division of the costal cartilage. This affords unparalleled access and exposure for the surgeon and facilitates ligation of the veins from the tumor. Troublesome bleeding occasionally encountered from the vena cava is also more easily controlled. Also with this approach there is minimal palpation of the tumor mass during the dissection. This is an important consideration because, besides the likelihood of causing severe hypertension, palpation can easily lacerate the thin fibrous capsule of a pheochromocytoma and allow extrusion of the soft vascular tumor tissue into the retroperitoneal space. In light of the fact that some 10 per cent of pheochromocytomas are malignant, excision should be as meticulous as any procedure for the removal of a tumor known to be malignant.

For dealing with a pheochromocytoma that cannot be demonstrated by radiographic studies to lie in the suprarenal areas or with a tumor suspected of being bilateral, we would prefer an elongated paramedian abdominal incision extending from xiphoid process to symphysis pubis. This again offers maximal exposure for exploration of both adrenal areas as well as the abdominal cavity. Since the tumor may lie in any area where chromaffin tissue is found, a thorough abdominal exploration, including close inspection of the great vessels and the base of the small bowel mesentery, is indicated. Pheochromocytomas have been found in the urinary bladder, in the chest and in other areas, but these are rare.

REPORTS OF CASES

CASE 1. A 46-year old white male truck driver was admitted to the University of California Hospitals on January 24, 1944. In the preceding four years he had had "spells" consisting of dizziness, nervousness, palpitations, a slow, pounding pulse, headache and occasional nausea and vomiting. These episodes occurred about five times a day and lasted 8 to 10 minutes. The diagnosis at that time was acute anx-

iety state with hyperventilation syndrome and the patient was referred to the psychiatric clinic.

The patient was readmitted on January 15, 1947, after being observed in a typical attack in a physician's office. The patient had suddenly become anxious, his head and neck became cyanotic and his blood pressure rose from 150/90 to 250/110 mm. of mercury and then dropped to normal 3 minutes after the attack began.

No abnormalities were noted on physical examination. The blood pressure was 160/80 mm. of mercury and the pulse rate 64. The results of routine laboratory tests were within normal limits. A histamine test was positive for pheochromocytoma. A glucose tolerance test was positive for increased epinephrine production. An electrocardiogram was interpreted as showing left ventricular hypertrophy, and in intravenous pyelograms a large right suprarenal mass was seen pressing the right kidney downward and laterally.

On February 1, 1947, through an incision over the bed of the twelfth rib, a pheochromocytoma lying beneath the remains of a grossly normal right adrenal was excised. The tumor weighed 490 gm. and contained 200 ml. of bloody fluid within a large cyst.

The postoperative course was fairly smooth and the patient was having no symptoms when he was discharged on the 17th postoperative day. As of his last letter in November, 1958, the patient continued to feel well and had worked steadily since discharge.

CASE 2. A 25-year old white housewife who was admitted to the University of California Hospitals on March 11, 1948, had been in excellent health until two and a half years before when she had episodes of blurry vision lasting 10 or 15 minutes, occasionally accompanied by typical Jacksonian seizures beginning in the left hand and associated with syncope. She was told by a physician on one occasion that her blood pressure during an attack was 240. Shortly before admission she began to have frequent occipital headaches, tinnitus, dyspnea on exertion and palpitations. She had had about 12 such attacks.

At the time of the physical examination the patient was noted to be slender and nervous and apparently not in acute distress. The blood pressure was 186/130 mm. and the pulse rate 108. The skin was flushed and the patient was perspiring. A loud systolic murmur and precordial thrust were noted. Routine laboratory tests revealed no abnormalities. An electrocardiogram was interpreted as showing left ventricular hypertrophy and sinus tachycardia.

A diagnosis of essential hypertension was made and a first stage left thoracolumbar sympathectomy was done March 17, 1948. On April 8, 1948, during the second stage right sympathectomy, a pheochromocytoma about 4 cm. in diameter lying just beneath a normal appearing right adrenal was discovered and excised. Symptoms did not recur in ten years of observation.

CASE 3. A 35-year-old white housewife, first admitted to the University of California Hospitals on May 15, 1952, said that she had had hypertension for three years. It was discovered first at the time of her first pregnancy. Later the patient experienced excessive perspiration, insomnia, nervousness and irritability, which had begun during her second pregnancy the following year. She also became aware of thirst, polyphagia, frequency of urination and moderate intolerance of heat. Previous to admission to hospital, a diagnosis of hyperthroidism had been made (basal metabolic rate of plus 72), and the patient had been given propylthiouracil under her physician's care, but her condition did not improve.

On physical examination it was noted that the patient was pale and obese. She perspired profusely and had cold clammy skin. The blood pressure was 130/90 mm. of mercury and the pulse rate was 110.

Results of routine laboratory tests were within normal limits. Intravenous pyelograms showed possible enlargement of the left adrenal gland. Results of cold pressor, benzodioxane and mecholyl tests were negative for pheochromocytoma. No abnormality was noted in a retroperitoneal oxygen study. Following mecholyl injection, the patient had crushing substernal pain; later, electrocardiographic changes suggested myocardial infarction. The patient then left the hospital against medical advice.

She was readmitted July 15, 1953, with progressive and severe symptoms of sweating, headache and impairment of vision of the right eye of one week's duration. A Regitine® test at this time was positive for pheochromocytoma. Intravenous pyelograms and retroperitoneal oxygen studies revealed a 7 cm. mass overlying the left kidney and displacing its upper pole laterally.

While awaiting operation, the patient noted beginning impairment of vision of her left eye. Intramuscular administration of 5 mg. of Regitine® every 6 hours was started to control hypertension.

On August 13, 1953, through a left Garlock transdiaphragmatic incision in the 9-10 interspace a well-encapsulated pheochromocytoma overlying the anterior aspect of the renal pedicle was removed. The tumor weighed 67 gm. and was 6.5 cm. in diameter. As the adrenal gland appeared to be normal and entirely separate from the tumor, it was not removed.

It was necessary to give Levophed® intravenously only during the first postoperative day and the patient was discharged on the ninth postoperative day.

When last examined in October, 1958, she had no symptoms and the blood pressure was 110/70 mm.

CASE 4. A 43-year-old white male pharmacist who was admitted to St. Luke's Hospital, San Francisco, on April 2, 1954, had had intermittent and severe attacks of nervousness, sweating, palpitations, upper abdominal discomfort and flushing of the face over a period of two years. The attacks lasted 10 to 20 minutes and occurred at about weekly intervals.

On physical examination this patient was observed to be nervous and hyperactive. The blood pressure was 160/110 mm. of mercury and the pulse rate 112. The facial skin was flushed, while that over the knees and elbows was decidedly cyanotic in blotchy areas. An active precordial heave was present.

On the second hospital day the blood pressure was 235/135 mm., then fell to 160/105 mm. within 10 minutes. During this hypertensive phase the patient was anxious and perspired profusely.

Abnormalities noted in laboratory tests included 4 plus proteinuria, leukocytes numbering 20,000 per cu. mm. A basal metabolic rate of +47, blood sugar content (fasting) 137 mg. per 100 cc. and nonprotein nitrogen of 65 mg. per 100 cc. The Regitine® test was positive for pheochromocytoma. A retroperitoneal oxygen study revealed a large tumor mass overlying the superior pole of the right kidney (Figure 1). The left adrenal gland was believed to be of normal size, although visualization was hampered by dilated loops of bowel.

On April 6, through a right Garlock transdiaphragmatic approach, a 200 gm. ovoid tumor measuring 10 x 8 x 4 cm. and enclosed by a thin ragged capsule was removed. The pathologist reported the tumor to be a malignant pheochromocytoma, with tumor cells invading the adrenal cortex.

It was necessary to maintain the patient's blood pressure with Levophed® until the fourth postoperative day when episodes of pronounced hypertension developed (blood pressure 240/170 mm. of mercury) with sweating, pallor, anxiety and increasing abdominal distention. X-ray examination with oxygen insufflation was repeated on April 16, and another large ovoid tumor mass was seen overlying the upper pole of the left kidney. This tumor had previously been erroneously thought to be a loop of bowel. The patient's family refused further operation, and death due to congestive heart failure followed within a week.

At autopsy a pheochromocytoma of about the same size as the one found on the right side, was observed above the kidney on the left. Hepatic metastatic lesions presumably secondary to the malignant right pheochromocytoma were also discovered.

CASE 5. A 71-year-old white woman entered St. Luke's Hospital, San Francisco, on March 5, 1955. She had had increasing attacks of nervousness, weakness, sweating, flushing, thirst and a ten-year history of poorly controlled diabetes mellitus and hypertension.

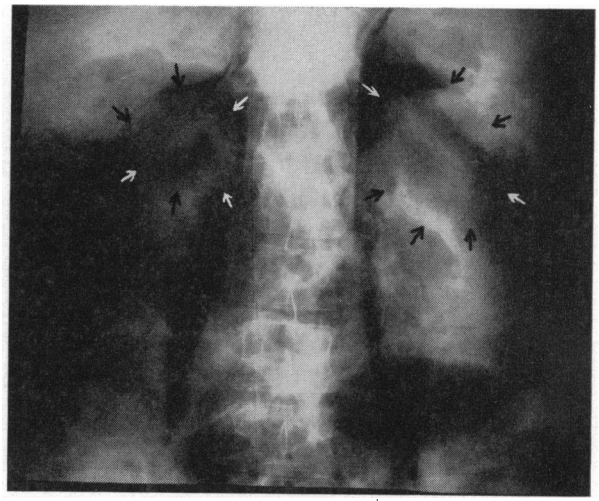

Figure 1 (Case 4)—Retroperitoneal oxygen study showing large bilateral pheochromocytomas. The left tumor was at first mistaken for a segment of dilated bowel.

Upon physical examination she was observed to be thin, prostrated and sweating profusely. The blood pressure was 210/110 mm. of mercury and the pulse rate 120. Except for evidence of cardiac enlargement no other abnormalities were noted. The blood sugar (fasting) was 296 mg. per 100 cc. and results of Regitine® and benzodioxan tests were positive. Intravenous pyelograms and retroperitoneal oxygen studies showed a mass 7 cm. in diameter overlying the superior pole of the left kidney.

On March 24, 1955, a 45 gm. pheochromocytoma was removed through a Garlock transdiaphragmatic incision between the ninth and tenth ribs. It was necessary to give Levophed® by slow infusion until the third postoperative day, and thereafter the course was uneventful. The patient was discharged from the hospital on the 21st postoperative day, with no symptoms. When she was examined thereafter no evidence of recurrence of the previous symptoms or glycosuria were noted and the blood pressure was within normal limits.

CASE 6. A 17-year-old white girl was admitted to the University of California Hospitals on July 6, 1955, with a history of intermittent attacks one to nine times a day consisting of headache, palpitations, nausea, vomiting, a sensation of numbness and paresthesia in both lower extremities, and sweating. These episodes lasted 3 to 10 minutes.

Her father had died at age 57 of a "stroke" and at autopsy was found to have bilateral pheochromocytomas. Her brother (see following case) also was later found to have a pheochromocytoma.

No abnormalities were noted upon physical examination. The blood pressure at the start of the examination was 160/90 mm. of mercury but rose shortly to 225/130 mm., and the rise was accompanied by substernal pain and sweating.

Results of laboratory studies were within normal limits. An electrocardiogram tracing was abnormal but nonspecific. The catechol assay of a 24-hour urine collection was 1,000 micrograms.

On July 13, 1955, a 250-gram pheochromocytoma was removed from the left adrenal area through a left Garlock transdiaphragmatic incision between the ninth and tenth ribs. The postoperative course was uneventful and vasopressors were not required.

A year and a half after the patient was discharged from the hospital, transient episodes of weakness, occasional headache and light-headedness, lasting 2 to 3 minutes, developed. Further studies were done but no evidence of another pheochromocytoma was found.

CASE 7. A 20-year-old white man, a laboratory technician, was admitted to the University of California Hospitals on July 9, 1955, at the prompting of his sister (see Case 6) because of a three-year history of recurrent attacks of palpitations, blanching of face and hands, tremor, numbness and tingling of the lower extremities and sweating. The attacks occurred 10 to 15 times a week and were of 5 to 20 minutes' duration. His sister had just been operated on for removal of pheochromocytoma at this hospital and his father at age 57 had died as the result of a cerebral vascular accident as a complication to bilateral pheochromocytomas discovered at autopsy.

On physical examination he appeared to be healthy and in no acute distress. The blood pressure was 135/80 mm. of mercury and the pulse rate 80. A grade II apical blowing systolic murmur was the only abnormality noted. Results of routine laboratory tests were within normal limits and no abnormalities were observed in pyelograms or in a retroperitoneal oxygen study. The results of a histamine test, glucose tolerance test and urinary catechols on two occasions were equivocal. The patient was discharged without a diagnosis of pheochromocytoma having been made.

He was readmitted on December 2, 1957, with complaint of more severe symptoms and more frequent attacks. A histamine test was strongly positive for pheochromocytoma; the blood pressure rose to 230/130 mm. of mercury from 120/80. Again intravenous pyelograms and retroperitoneal oxygen studies showed no abnormalities but an aortogram revealed a small tumor in the region of the right adrenal gland. On December 19, 1957, a 3 x 1.5 x 1.5 cm. pheochromocytoma was removed from the right suprarenal area through a right Garlock transdiaphragmatic incision between the ninth and tenth ribs. The patient made an excellent recovery and vasopressors were not given postoperatively. When last examined, in November, 1958, he was asymptomatic. The blood pressure was 120/85 mm.

CASE 8.* A 55-year-old white housewife was admitted to the University of California Hospitals on March 10, 1956, because of severe headaches, warm flushes and "choking sensations" during the preceding six months. These episodes occurred daily, usually lasting 5 minutes, and were precipitated when she lay on her left side. She had undergone total left and partial right adrenalectomy previously for Cushing's syndrome. At that time severe diabetes, virilization, with elevated 17 ketosteroids and 17 hydroxycorticoids had been noted and the diagnosis of Achard-Tiers syndrome had been made.

On physical examination the patient appeared to be healthy and to have no residual of Cushing's syndrome. The blood pressure was 165/85 mm. of mercury and the pulse rate was 88. There were no remarkable physical findings.

No abnormalities were seen in retroperitoneal oxygen studies. The basal metabolism rate and an electrocardiogram were within normal limits.

Shortly after admission the patient had an attack of hypertension, with blood pressure at 240/180 mm. of mercury for 10 minutes. A subsequent Regitine® test was positive for pheochromocytoma and urinary catechols were 1,100 micrograms in a 24-hour urine collection.

On March 27, 1956, the patient underwent operation, and through an upper transverse abdominal incision a pheochromocytoma 5 cm. in diameter that lay amidst the remnants of the right adrenal gland and was intimately adherent to the vena cava was removed. The patient made an uneventful recovery. Vasopressors were given until the fourth postoperative day. The patient was maintained on complete adrenal cortical replacement therapy, and when examined 20 months after the operation was having no symptoms. The blood pressure was 110/80 mm.

CASE 9.† A 59-year-old white male school teacher was admitted to the University of California Hospitals on June 17, 1956. For a year he had had paroxysmal bouts of palpitations, headaches, spots before his eyes, substernal ache, dizziness, weakness and tremor. The attacks varied in intensity, lasted 1 to 30 minutes and occurred at least once daily.

On physical examination the patient was observed to be thin. The blood pressure was 120/70 mm. of mercury and the pulse rate was 72. During rectal examination a typical attack suddenly developed with

*Courtesy of Doctors Peter Forsham and Maurice Galante.
†Courtesy of Dr. Frank Hinman, Jr.

a rise in blood pressure to 260/150 mm. This episode lasted 20 minutes.

A hemogram, urinalysis, fasting blood sugar and protein bound iodine were within normal limits. A urinary catechols assay revealed a borderline elevation of 160 micrograms in 24 hours. Histamine and Regitine® tests were positive for pheochromocytoma.

Tomograms of the adrenal glands suggested a tumor mass in the right adrenal area. In a retroperitoneal oxygen study an ovoid tumor 3 cm. in diameter was seen lying adjacent to the right adrenal.

On June 26, 1956, a right Garlock transdiaphragmatic incision was made between the ninth and tenth ribs and a pheochromocytoma 3 cm. in diameter lying posterior and medial to the adrenal gland was excised together with the right adrenal. The specimen weighed 19 gm.

The patient was dismissed from the hospital asymptomatic and with a blood pressure of 110/70 mm. of mercury on the tenth postoperative day.

Two years later he was readmitted to this hospital for transurethral prostatectomy. The blood pressure at that time was 120/80 mm. of mercury. The course of his stay in hospital was entirely uneventful.

CASE 10.‡ A 35-year-old white housewife admitted to the University of California Hospitals on March 30, 1957, complained of paroxysmal attacks of epigastric pain, palpitations, sweating and headaches occurring at very irregular intervals during the preceding two years and lasting 5 to 20 minutes. The physician who referred her had noted a labile blood pressure varying from 140/95 to 190/110 mm. of mercury during one visit.

The patient was an anxious, hyperreactive, well developed woman. The blood pressure was 125/90 mm. of mercury and the pulse rate 100. Upon cardiac examination, a forceful ventricular heave, cardiac enlargement and a systolic apical murmur were noted. An electrocardiogram revealed anterior myocardial ischemia. A hemogram and results of urinalysis were within normal limits. Results of histamine and Regitine® tests were positive for pheochromocytoma and the excretion of urinary catechols was reported to be 1,000 micrograms in 24 hours. Intravenous pyelograms and retroperitoneal oxygen studies revealed slight downward and lateral displacement of the upper pole of the kidney with a tumor mass 10 cm. in diameter lying just anterior to the kidney. On April 9, 1957, the patient was taken to the operating room, but immediately after she was transferred to the operating table, it became apparent that she had had incomplete right hemiparesis. The operation was postponed for ten days, the hemiparesis having almost disappeared by then. Through an extra-pleural eleventh rib approach a pheochromocytoma about 10 cm. in diameter was removed. Vasopressors were used until the third postoperative day. The patient was dismissed from the hospital asymptomatic on the 16th postoperative day. The blood pressure was then 110/70 mm. of mercury, and urinary catechol content was normal. She received physiotherapy for slight residual of the right hemiparesis.

‡Courtesy of Dr. Frank Hinman, Jr.

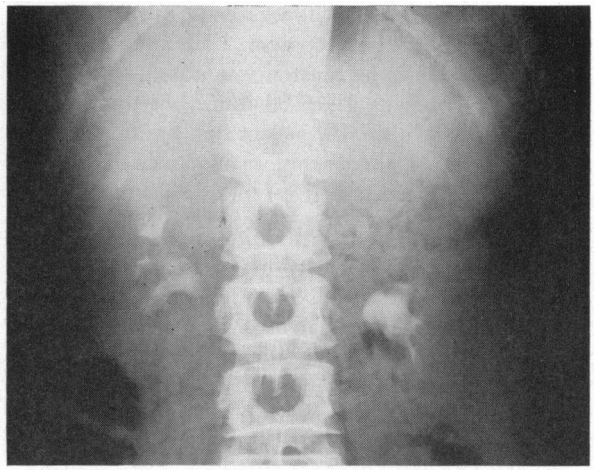

Figure 2 (Case 11)—Pyelogram demonstrating downward and lateral displacement of left kidney from a suprarenal mass.

CASE 11. A 53-year-old white saleswoman was admitted to the University of California Hospitals on June 15, 1957. She had had recurrent attacks of dizziness, weakness, palpitations, sweating, and headaches with occasional nausea and vomiting in the preceding four months. She said she had been "nervous" all of her life and had been told she was hypertensive five years before. The attacks occurred two to three times a day and lasted 10 to 30 minutes.

The patient was thin and anxious. The blood pressure was 160/85 mm. of mercury and the pulse rate 100. There was evidence of cardiomegaly and a Grade II systolic murmur was heard over the precordium. The results of urinalysis and of a hemogram were within normal limits. Significant findings included a Regitine® test positive for pheochromocytoma. The content of catechols in a 24-hour specimen of urine was 500 micrograms. During intravenous pyelograms the patient's blood pressure soared suddenly to 250/170 mm. and she had a typical attack. The pyelograms showed a suprarenal mass 10 cm. diameter displacing the left kidney downward (Figure 2). On June 28, 1957, through a left Garlock transdiaphragmatic incision, a large pheochromocytoma was removed. It was necessary to give the patient 400 mg. of Regitine® intravenously during a two-hour period in the operating room before the blood pressure descended to a level permitting induction of anesthesia. Levophed® drip was required

for only two hours postoperatively, and the postoperative course was benign. Four months after operation labile hypertension was noted, with blood pressure as high as 190/100 mm., but the urinary catechol assay was within normal limits. No evidence of another pheochromocytoma was discovered and the patient remained essentially asymptomatic.

CASE 12. A 17-year-old white single female was admitted to the University of California Hospitals on December 21, 1958. Four months previously, sweating, dizziness and nausea had occurred when she was singing in church. She also noted substernal pain, aggravated by exercise or deep breathing, as well as polydipsia and severe frontal headaches and night sweats. These attacks usually persisted for 1 to 3 minutes. This condition had been diagnosed as diabetes by a physician six weeks before her admission to the hospital, and she had been found to have Kimmelstiel-Wilson retinopathy and an abnormal glucose tolerance curve.

The patient was normal-looking and apparently in no acute distress, with a blood pressure of 150/110 mm. and a pulse rate of 80. The skin was generally moist. On examination of the eyegrounds, flame shaped hemorrhages, exudates and papilledema of the left fundus were noted. Cardiac examination revealed a precordial thrust and a Grade I systolic blowing murmur at the apex.

Leukocytes numbered 15,000 per cu. mm. of blood, 80 per cent polymorphonuclear cells. The sedimentation rate was 22 mm. in one hour. The basal metabolism rate was plus 52. A Regitine® test was strongly positive for pheochromocytoma. The plasma norepinephrine was elevated to 16 micrograms/liter and the plasma epinephrine to .58 micrograms/liter. The only abnormality observed in intravenous pyelograms was a slight axis deviation on the right, but retroperitoneal oxygen studies revealed a mass measuring 6 x 5 x 4 cm. overlying the right kidney in the adrenal area (Figure 3).

On December 30, 1958, a pheochromocytoma intimately adherent to the right adrenal was removed through a right Garlock transdiaphragmatic incision. The tumor weighed 30 gm. It was not necessary to give vasopressors postoperatively, and the patient's blood pressure stabilized at 170/100 mm. of mercury. Results of histamine and Regitine® tests and urinary catechol assay after operation did not suggest the presence of another pheochromocytoma.

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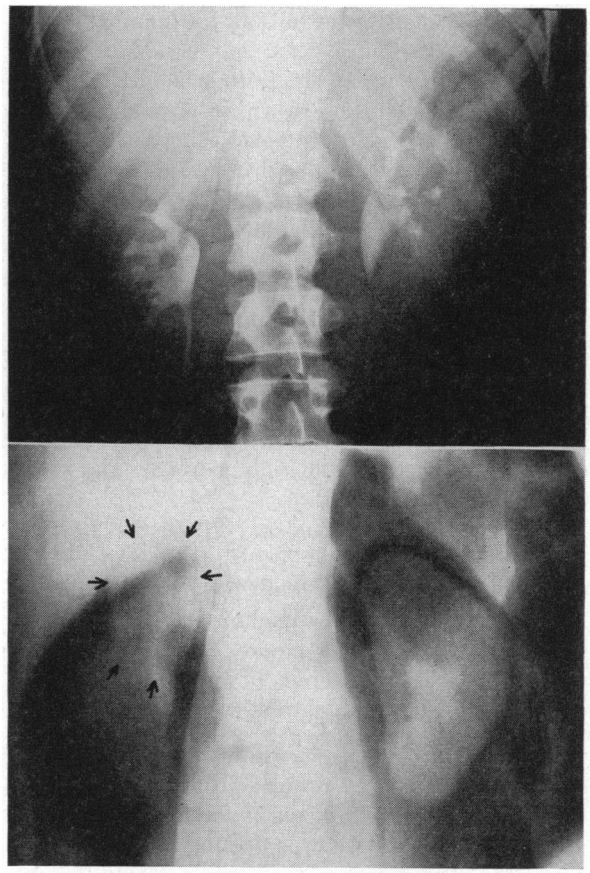

Figure 3 (Case 12)—*Above:* Pyelogram revealing abnormal vertical calyceal axis of right kidney and normal oblique axis on left. *Lower:* Retroperitoneal oxygen study showing right pheochromocytoma.

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